



## Combined oxidative phosphorylation deficiency 1

Combined oxidative phosphorylation deficiency 1 is a severe condition that primarily impairs neurological and liver function.

Most people with combined oxidative phosphorylation deficiency 1 have severe brain dysfunction (encephalopathy) that worsens over time; they also have difficulty growing and gaining weight at the expected rate (failure to thrive). In some cases, affected individuals have abnormal muscle tone (increased or decreased), developmental delay, seizures, loss of sensation in the limbs (peripheral neuropathy), and an unusually small head (microcephaly). Liver disease is common in people with combined oxidative phosphorylation deficiency 1, with individuals quickly developing liver failure. Individuals with this condition also usually have a potentially life-threatening buildup of a chemical called lactic acid in the body (lactic acidosis).

The neurological features of combined oxidative phosphorylation deficiency 1 are largely due to brain abnormalities that include thinning of the tissue that connects the two halves of the brain (corpus callosum hypoplasia) and loss of brain tissue called white matter (leukodystrophy), particularly in an area of the brain called the basal ganglia, which normally helps control movement.

Individuals with combined oxidative phosphorylation deficiency 1 usually do not survive past early childhood, although some people live longer.

### Frequency

Combined oxidative phosphorylation deficiency 1 is likely a rare disorder, although its prevalence is unknown. At least 12 affected individuals have been described in the scientific literature.

### Causes

Combined oxidative phosphorylation deficiency 1 is caused by mutations in the *GFM1* gene. This gene provides instructions for making an enzyme called mitochondrial translation elongation factor G1. This enzyme is found in cell structures called mitochondria, which are the energy-producing centers in cells.

While instructions for making most of the body's proteins are found in DNA that is stored in the nucleus of cells (nuclear DNA), a few proteins and other molecules are produced from DNA that is stored in mitochondria (mtDNA). Mitochondrial translation elongation factor G1 is involved in the production of proteins from mtDNA genes through a process called translation. The enzyme's role in translation is to coordinate the movements of mtRNA molecules, which are the protein blueprints created from mtDNA. This function allows assembly of proteins to continue until it is complete. Genes

on mtDNA provide instructions for proteins that are primarily involved in the process of converting the energy from food into a form cells can use (oxidative phosphorylation).

*GFM1* gene mutations reduce or eliminate mitochondrial translation elongation factor G1 function. As a result, fewer mitochondrial proteins involved in oxidative phosphorylation are produced. (The process of oxidative phosphorylation involves five groups of proteins, or complexes. The condition is called combined oxidative phosphorylation deficiency 1 because it impairs the function of more than one of these complexes.) Organs that have high energy demands, such as the brain and liver, are particularly affected by the resulting impairment of oxidative phosphorylation. A shortage of energy in these tissues leads to cell death, causing the neurological and liver problems in people with combined oxidative phosphorylation deficiency 1. It is thought that other tissues that require a lot of energy, such as the heart and other muscles, are not affected in this condition because they have additional enzymes that can perform the process of mitochondrial protein production.

## **Inheritance Pattern**

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

## **Other Names for This Condition**

- COXPD1
- early fatal progressive hepatoenkephalopathy
- hepatoenkephalopathy due to combined oxidative phosphorylation defect type 1

## **Diagnosis & Management**

### Genetic Testing Information

- What is genetic testing?  
[/primer/testing/genetic-testing](#)
- Genetic Testing Registry: Combined oxidative phosphorylation deficiency 1  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C183679/>

## **Additional Information & Resources**

### Health Information from MedlinePlus

- Encyclopedia: Lactic Acidosis  
<https://medlineplus.gov/ency/article/000391.htm>
- Health Topic: Mitochondrial Diseases  
<https://medlineplus.gov/mitochondrialdiseases.html>

### Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Encephalopathy Information Page  
<https://www.ninds.nih.gov/Disorders/All-Disorders/Encephalopathy-Information-Page>

### Educational Resources

- Boston Children's Hospital: Mitochondrial Disease in Children  
<http://www.childrenshospital.org/conditions-and-treatments/conditions/m/mitochondrial-disease>
- Children's Hospital of Philadelphia: What is Mitochondrial Disease?  
<https://www.chop.edu/conditions-diseases/mitochondrial-disease>
- Cincinnati Children's Hospital: Mitochondrial Disorders Program  
<https://www.cincinnatichildrens.org/service/m/mitochondrial-disorders>
- Kennedy Krieger Institute: Mitochondrial Disorders  
<https://www.kennedykrieger.org/patient-care/conditions/mitochondrial-disorders>
- MalaCards: combined oxidative phosphorylation deficiency 1  
[https://www.malacards.org/card/combined\\_oxidative\\_phosphorylation\\_deficiency\\_1](https://www.malacards.org/card/combined_oxidative_phosphorylation_deficiency_1)
- Merck Manual Consumer Version: Acidosis  
<https://www.merckmanuals.com/home/hormonal-and-metabolic-disorders/acid-base-balance/acidosis>
- Orphanet: Hepatoencephalopathy due to combined oxidative phosphorylation defect type 1  
[https://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=137681](https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=137681)

### Patient Support and Advocacy Resources

- American Liver Foundation  
<https://liverfoundation.org/>
- Child Neurology Foundation  
<https://www.childneurologyfoundation.org/>
- MitoAction  
<https://www.mitoaction.org/>
- United Mitochondrial Disease Foundation  
<https://www.umdf.org/>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28combined+oxidative+phosphorylation+deficiency%29+AND+%28EFG1%29+OR+%28GFM1%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

### Catalog of Genes and Diseases from OMIM

- COMBINED OXIDATIVE PHOSPHORYLATION DEFICIENCY 1  
<http://omim.org/entry/609060>

### Medical Genetics Database from MedGen

- Combined oxidative phosphorylation deficiency 1  
<https://www.ncbi.nlm.nih.gov/medgen/322999>

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